Claim 50, line 2, please change "an antigen" to --vP9--.

**REMARKS**

The Examiner is thanked for the courtesies extended during the Interview of August 31, 1995 wherein the Examiner agreed that vP2, vP4 and vP6 are three distinct species within claim 42.

Reconsideration and withdrawal of the rejections of this application, withdrawal of the finality of the July 12, 1995 Office Action, as well as withdrawal of that Office Action, the addition of this application to Interference No. 103,399, designation of claims 33 to 51 as corresponding to the Count, substitution of claim 42 as the Count, and redeclaration of the Interference with Paoletti as Senior Party, are respectfully requested. To any extent necessary, this paper is to be considered a Petition For Withdrawal of Finality, as well as a Petition for Consideration After Final Rejection under 37 C.F.R. §1.129(a). The Commissioner is hereby authorized to charge any requisite fee for such petitions to Deposit Account No. 03-3925.



**THE OFFICE ACTION IS INCOMPLETE AND THEREFORE FINALITY IS IMPROPER**

The Office Action asserts that claims 33 to 48, 50 and 51 "do not correspond to the pending interference count, because

they do not contain the element of the promoter being 'adjacent to' the foreign sequence" (Office Action, at 2).

The Office Action FAILS to define "promoter" or "adjacent to" or "foreign sequence". Thus, the Office Action FAILS to show how any of vP2, vP4 or vP6, or any of claims 33 to 48, 50 and 51 do not inherently or explicitly "contain the element of the promoter being 'adjacent to' the foreign sequence."

Accordingly, the Office Action is incomplete; finality is improper. The Office Action and the finality thereor should be withdrawn, and such relief is respectfully requested.

Indeed, the meaning of each of "promoter", "adjacent to" and "foreign gene" are key issues in Interference No. 103,399, thereby furthering the proposition below that the application should be added to the Interference, and the Office Action and finality thereof withdrawn, with the APJ and Board deciding the issues. In particular, Paoletti et al. has asserted in the Interference that Moss et al. has varied the meanings for "foreign gene" and "promoter"; and that Moss et al. has failed to define "adjacent to".

More specifically, in Moss et al. USSN 06/445,451, "foreign gene" was defined to "include the site corresponding to initiation of translation" whereas in Moss et al. USSN 07/072,455, the "foreign gene" only "may" include the site corresponding to initiation of translation.

In Moss et al. USSN 06/445,451, a "promoter" was defined as DNA preceding and including the site at which RNA synthesis begins, whereas in Moss et al. USSN 07/072,455, a "promoter" is broadly, and functionally, defined at page 2, lines 2-3 as any "sequence that positively regulate[s] ... transcription of a gene" and only "may" include the site at which RNA synthesis begins. Therefore, a "promoter" as defined in USSN 06/445,451 is a longer piece of DNA than the shorter length DNA permitted by the broadened "promoter" definition in USSN 07/072,455). Since Moss' functional definition of "promoter" in USSN 07/072,455 is such that DNA which does not so function, such as any extraneous intervening HSV-TK DNA in vP2, vP4 and vP6 is excluded, Paoletti's "under vaccinia control" language meets Moss' promoter definition.

Furthermore, the meaning of the term "adjacent to" is unclear in and not described, enabled or defined by the Moss et al. applications. Examiner Mosher, during the prosecution of Moss et al. USSN 07/987,456, in a June 24, 1993 Office Action, keenly asserted that, "The instant [Moss et al.] specification does not explicitly define 'adjacent'". Indeed, during that prosecution Examiner Mosher supplied her own definition for "adjacent", albeit, it is respectfully submitted, incorrectly, since she employed Webster's Dictionary, as opposed to the concept of "adjacent" from the prior art, e.g., Venkatesan, Cell 125:805-13, 1981.

In the prior art, such as Venkatesan, supra, the term "adjacent to" is used to exclude any intervening nucleotides. Accordingly, the Moss et al. applications do not enable the term "adjacent to" because, as discussed in papers filed in the Interference, all of the Moss et al. application Examples and disclosure are directed to constructs having extraneous DNA sequences between the vaccinia promoter element and the translation initiation site of the foreign gene. Thus, Moss' "adjacent" is undefined, allows for the presence of extraneous intervening DNA, and merely means purposeful placement of a foreign gene and promoter DNA. Such a meaning is met by Paoletti's "operably linked ... which exerts functional control ... wherein there is expression of the donor DNA under vaccinia control."

If the dictionary definition is used to define "adjacent" as "the absence of anything of the same kind in between", then Moss' (and the Count's) "adjacent to" excludes a vaccinia promoter intervening between the recited vaccinia promoter and the recited foreign gene. Moss' (and the Count's) "adjacent" does not exclude extraneous exogenous DNA which, in a vaccinia setting, is inoperative as a promoter, even though in a herpes simplex virus setting it would act as a promoter (since "promoter" is a functional definition of a particular DNA sequence; if the DNA does not function as a "promoter" it is not a promoter). See also USSN 07/072,455, page 1, line 22 to page

2, line 5 (promoter defined as a sequence which "positively regulate[s] the transcription of a gene" such that Moss' application, by its own terms, prevents "adjacent" from excluding the additionally inoperative HSV TK DNA of Paoletti's vP2, vP4 and vP6).

The dictionary definition of "adjacent," by excluding an intervening vaccinia promoter, also does not exclude an intervening vaccinia coding sequence, contrary to the positions of Moss and Examiner Mosher. Note that in the Count and each of Moss' claims 33, 44, 55 and 57, the phrase "said promoter sequence is adjacent to" refers to the earlier recited "vaccinia virus promoter sequence" such that "absence of anything of the same kind in between", according to the dictionary, only excludes an intervening vaccinia virus promoter sequence (or an intervening sequence coding entirely for a foreign polypeptide).

Note further that Cochran et al., J. Virol. 59(1):30-37 (April 1985) (of record in the Interference and a copy of which will be supplied upon request) disclose that there are "independent early and late RNA start sites within the promoter region of the 7.5-kD gene," such that Moss' Examples and claims do not meet Webster's definition for "adjacent" since the Moss 7.5 promoter containing recombinants have a proximal RNA start site (promoter) between a distal RNA start site (promoter) and the foreign coding sequence, i.e., there is an intervening promoter in those recombinants, contrary to the dictionary

definition of "adjacent to". Because the meaning of "adjacent to" in the Moss application is unclear, and the resolution of this issue is one of the key issues in Interference No. 103,399, it is respectfully submitted that it is inappropriate for the present application to be excluded from the Interference for not containing the element of the promoter being "adjacent to" the foreign sequence. Accordingly, it is respectfully requested that the Examiner reconsider and withdraw the Office Action and add this application to the Interference with claims 33 to 51 designated as corresponding to the Count.

With respect to either the Count or Proposed Count A (Paoletti claim 42), Paoletti, in Interference No. 103,399, identified and respectfully requested the benefit of the filing date of:

(1) USSN 08/228,926, filed April 18, 1994 and pending.

(2) USSN 07/881,995, filed May 4, 1992.

(3) USSN 537,882, filed June 14, 1990, now U.S. Patent No. 5,110,587.

(4) USSN 90,209, filed August 27, 1987.

(5) USSN 622,135, filed June 19, 1984, now U.S. Patent No. 4,722,040.

(6) USSN 446,825, filed December 8, 1982, now U.S. Patent No. 4,603,112.

(7) USSN 334,456, filed December 24, 1981, now U.S. Patent No. 4,769,330 ("the '330 Patent").

Moss has not challenged that Paoletti is entitled to the benefit of all of these applications with respect to Proposed Count A (Paoletti claim 42), and the APJ and Board have not yet rendered a decision on Paoletti's request. Thus, it is improper for the Examiner to attempt to decide this issue in the Office Action.

To be entitled to the benefit of USSN 334,456, Paoletti need only show that the application complies with 35 U.S.C. §112, first paragraph with respect to at least one embodiment within the scope of the Count. See Weil v. Fritz, 196 U.S.P.Q. 600, 608 n.16 (C.C.P.A. 1978).

vP2, vP4 and vP6, and the "further embodiment" disclosed at column 15, lines 3 to 20 of the '330 Patent, all meet the terms of the Count, Moss claim 44, under Moss' new-found definition for "adjacent to." Note also the teaching of deliberate placement with respect to a "strong promoter" at column 2, line 63 to column 3, line 1 of the '330 Patent and that the promoter is a vaccinia promoter in view of column 10, line 10 teaching expression under vaccinia control.

Moss claim 44 (the Count) reads:

> A recombinant vaccinia virus that comprises a segment comprised of (A) a first DNA sequence encoding a polypeptide that is foreign to vaccinia virus and (B) a vaccinia promoter sequence, wherein (i) said promoter sequence is adjacent to and exerts transcriptional control over said first DNA sequence and (ii) said segment is positioned

Moss defines a "promoter" as "sequences that positively regulate the transcription of a gene" (USSN 07/072,455, at page

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> within a nonessential genomic region of said recombinant vaccinia virus.

With respect to the undefined term "adjacent to", from the possible definitions[1] Moss now asserts that it "means that there can be no intervening promoter between the recited vaccinia promoter and the foreign gene" (Moss Opposition to Paoletti Motion for Unpatentability Due to Lack of Enablement and Written Description, at 8).

Further, Moss "emphasizes that it has never explicitly or implicitly indicated that ['adjacent to' excludes] 'extraneous exogenous DNA'" (Id. at 34). In other words, Moss has asserted that "adjacent to" does not mean that the promoter and foreign gene are contiguous or in contact; but rather, that the term "adjacent to" permits and calls for the presence of intervening extraneous exogenous DNA.[2]

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[1] See Venkatesan, Cell, 125:805-13, 1981 wherein "adjacent to" means contiguous; see also June 24, 1993 Office Action USSN 07/987,456, at 2-3: "adjacent may or may not imply contact but always implies absence of anything of the same kind in between". Note also that "said promoter" in Moss claim 44 refers to "a vaccinia promoter" such that "adjacent to" can also mean no intervening "vaccinia promoter"; ergo, if, as according to Moss the intervening extraneous HSV DNA in vP2, vP4 and vP6 is a "HSV promoter" (and such is not admitted herein), then vP2, vP4 and vP6 do not have an intervening "vaccinia promoter" excluded by "adjacent to" (and therefore vP2, vP4 and vP6 meet the terms of Moss claim 44).

[2] Accordingly, the plasmid in Example 4A of U.S. Patent No. 5,174,993 wherein the H6 promoter (referred to as HH for HindIII H) was superimposed on the initiation codon of the rabies G gene (no intervening extraneous DNA), and Examples 1, 10, 12, 13 and 14 of U.S. Patent No. 5,338,683 (H6/EHV gp13, vP483; H6/PRV gpII; H6/PRV g1; H6/HSV2 gB, H6/HSV2 gC, H6/HSV2 gD; H6/BHV1 gI; all without intervening extraneous DNA) are outside of Moss' claims. Note that U.S. Patent No. 5,338,683 was accorded a lineage under 35 U.S.C. §120 back to USSN 334,456, filed December 24, 1981, showing that the PTO has already decided that the '330 Patent does not require the presence of extraneous DNA which may function in the HSV context, contrary to Moss' bogus assertion that the '330 Patent somehow requires the presence of a

Moss defines a "promoter" as "sequences that positively regulate the transcription of a gene" (USSN 07/072,455, at page 2, lines 2-3), or as "a regulatory element that 'binds RNA polymerase and directs the enzyme to the correct transcriptional start site'" (See Moss' Opposition to Paoletti's Motion to Substitute a Count, at 15).

Inserting Moss' definitions into the Count, Moss claim 44, makes that claim read:

> A recombinant vaccinia virus that comprises a segment comprised of (A) a first DNA sequence encoding a polypeptide that is foreign to vaccinia virus and (B) a vaccinia **sequence that positively regulates transcription of a gene,** wherein (i) **said sequence that positively regulates transcription of a gene has no intervening sequence that positively regulates transcription of a gene between it and said first DNA sequence** and exerts transcriptional control over said first DNA sequence and (ii) said segment is positioned within a nonessential genomic region of said recombinant vaccinia virus.

In vP2, vP4 and vP6, the intervening extraneous HSV DNA is not a promoter in the vaccinia virus environment, does not function in the vaccinia virus environment as a promoter, i.e., to "positively regulate ... transcription", and could not function in the vaccinia virus environment to "positively regulate ... transcription".[3]

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HSV promoter.

[3] Moss asserts without any proof that the intervening extraneous HSV DNA in vP2, vP4 and vP6 is a promoter and could so act; but, as shown by the lack of expression in vP1, vP3 and vP5, the intervening extraneous HSV DNA in

Thus, vP2, vP4 and vP6 comprise a segment comprised of a first DNA sequence encoding a polypeptide foreign to vaccinia virus (HSV TK gene or coding sequence) and a vaccinia sequence that positively regulates transcription (vaccinia F7L promoter). The F7L promoter in vP2, vP4 and vP6 has no DNA sequence between it and the HSV TK gene (coding sequence) which regulates transcription of the HSV TK gene (coding sequence) in the vaccinia environment. And, the F7L promoter and HSV TK gene (coding sequence) in vP2, vP4 and vP6 are in a non-essential region of the vaccinia virus genome.

Furthermore, USSN 334,456 explicitly teaches that in view of expression of vP2, vP4 and vP6 and not by vP1, vP3 and vP5, that "the HSV TK-modified F-fragment is incorporated into the vaccinia variants in the cell and is then capable of replication and expression under vaccinia control" (see U.S. Patent No. 4,769,330, col. 10, lines 7 to 10; emphasis added).

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vP2, vP4 and vP6 has no particular coding or regulatory function and is thus merely extraneous exogenous DNA. Furthermore, note that the '330 Patent speaks of and teaches inserting the "HSV TK gene" (i.e., the HSV TK coding sequence without any "HSV promoter sites") into the HindIII F-fragment (see, e.g., col. 9, line 63 to col. 10, line 10). The '330 Patent distinguishes the "HSV TK gene" from the "Bam HSV TK fragment"; the latter containing the HSV TK gene and extraneous non-functioning DNA (as to vaccinia virus), the former not including that extraneous non-functioning DNA (note that only the "Bam HSV TK fragment" is identified as having that DNA, not also the "HSV TK gene"). Thus, the '330 Patent is not teaching any requirement that one must also insert any "HSV promoter sites (that) do exist within the Bam HSV TK fragment" (note too that they are identified in the '330 Patent not as a "promoter" but rather, as "HSV promoter sites", indicating that they are DNA which functions and is therefore a promoter in HSV but not in vaccinia virus). Thus, USSN 334,456 discloses in its general teachings as an exemplary embodiment inserting HSV TK gene into the HindIII F-fragment without the "HSV promoter sites", analogous to vP22.

This is clearly a teaching and enabling disclosure that expression of the foreign gene (the HSV TK gene) in the recombinant vaccinia virus (vP2, vP4 and vP6) was under the control of vaccinia regulatory sequences (promoter). Note again the teaching in column 2, line 63 to column 3, line 1 of the '330 Patent of deliberate placement with respect to or use of a "strong promoter" (which is a vaccinia promoter in view of column 10, lines 7 to 10).

Note additionally that USSN 334,456, in the further embodiment disclosed in U.S. Patent No. 4,769,330, column 15, lines 3 to 20, also recognizes that the endogenous promoter was operational (or that expression was under vaccinia control) and that there was not, as argued by Moss, reliance by Paoletti upon the presence of the "HSV promoter." In that further embodiment, the Bam HSV TK fragment incorporated into the HindIII F-fragment of VTK-79 is, by recombination, "replaced by an F-fragment containing [another] exogenous gene," such that the resultant recombinant does not have the "HSV promoter".

Thus, under Moss' new-found definition for "adjacent to" and Moss' own arguments, vP2, vP4 and vP6 and the above-mentioned "further embodiment" of USSN 334,456 are each embodiments within the Count, there is no requirement in USSN 334,456 for the presence of a "HSV promoter"; and placement of the foreign gene with respect to the vaccinia promoter can be

deliberate, contrary to Moss' misreading of U.S. Patent No. 4,769,330.

Accordingly, vP2, vP4, vP6 and the presently claimed subject matter indeed have the concept of "adjacent to" in the same manner as Moss. Alternatively, if "adjacent to" is used in the sense of Venkatesan, supra, neither Paoletti nor Moss have the concept of "adjacent to." Nonetheless, the Office Action is incomplete by failing to define "adjacent to", "promoter" and "foreign sequence". Simply, how can the Office Action assert that Applicants do not have "the promoter being 'adjacent to' the foreign sequence" when the Office Action does not define any of the "promoter", "adjacent to" and "foreign sequence"?

Reconsideration and withdrawal of the finality of the Office Action, and withdrawal of the Office Action altogether, are earnestly solicited (see also infra).

**CLAIM 40 IS CORRECTED**
**AND NEW CLAIM 50 AMENDED**

Claim 50 is amended to call for the recombinant vaccinia virus to be vP9. Claim 40 is amended by changing "pDP202" to --pDP202 TK/E-- (as that was the plasmid used to make vP22). No new matter is added. No additional search is required.

Reconsideration and withdrawal of the Section 112, fourth paragraph rejection (Office Action, at 3) are respectfully requested.

**CLAIMS ARE ENTITLED TO THE BENEFIT OF USSNs 06/334,456 AND 06/446,842 AND THE APPLICATION SHOULD BE ADDED TO THE INTERFERENCE**

As alluded to above, claims are entitled to the benefit of USSN 06/334,456 (now the '330 patent), and it is hereby respectfully requested that the Office Action be withdrawn in its entirety as the issues addressed therein are before the APJ and Board by the Interference and should be decided by the APJ and the Board; and, because the Office Action is incomplete.

More specifically, claim 49 (vP22) apparently in the Examiner's view has the concept of "adjacency" (since only claims 33 to 48, 50 and 51 are said to not contain "adjacent to"), claims 48 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting, claims are denied the benefit of USSN 06/334,456 and 06/446,824, claims 33, 34, 41, 42, 43, 50 and 51 are rejected under 35 U.S.C. §102(b) as anticipated by Mackett et al., claims 38, 47 and 49 are rejected under Section 103 as unpatentable over Mackett et al. in view of Panicali et al., claim 40 is rejected under Section 103 as obvious over Panicali et al., claim 39 (pDP137) is merely objected to, and claims 35 to 37 and 44 to 46 are merely objected to.

1. **The Application Can Be Passed To The Board**

The Office Action fails to state which filing date is being accorded to each specific claim; and therefore, the Office

Action is incomplete such that it and its finality should be withdrawn.

More particularly, the Office Action should explicitly state as to each claim which filing date is being accorded; for instance, the Office Action should state, "... claim 42 is accorded the benefit of USSN 06/344,456 ... claim 49, directed to vP22, is accorded the benefit of USSN 06/446,824 ..." Since the Office Action fails to state which date each claim was accorded, the Office Action is incomplete; and therefore, it and its finality should be withdrawn, and such relief is again respectfully requested.

Nonetheless, the application can be passed to the APJ and the Board.

vP22, claimed in claim 49, was clearly disclosed and enabled in USSN 06/446,824, filed December 8, 1982. Claim 49, vP22, apparently corresponds to the pending Count. Claim 49 is rejected for obviousness-type double patenting and under Section 103 based upon Mackett et al.

The filing of a Terminal Disclaimer will be considered after the issues of priority vis-a-vis Moss et al., and of Moss' patentability vis-a-vis Paoletti are resolved by way of the Interference. Note M.P.E.P. §2309.02 which provides: "The fact that a claim may be under rejection does not mean that it should not be designated." Accordingly, holding the double patenting rejection in abeyance is respectfully requested.

The undersigned had an investigation performed under his direction, supervision and control in the ordinary course of business as to the date of availability of the Mackett et al. article, and had also received the results of a similar investigation believed performed by persons on behalf of Mackett et al. in the context of a European Opposition. On information and belief, the mailing date, and ergo the date of availability, of the Mackett et al. article was December 8, 1982. It is hereby declared that this statement is made with the belief that it is true, and with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18, U.S.C., and that such willful false statements may jeopardize the validity of the application and any patent issued thereon. Thus, Mackett et al. is not prior art and the Section 102 and 103 rejections based on Mackett are therefore overcome.

Similarly, claim 48, directed to vP2, vP4 and vP6, is not rejected on the basis of any prior art (only on the basis of obviousness-type double patenting), and, as discussed above, vP2, vP4, and vP6 contain the element of "adjacency" (if "adjacent to" allows the presence of extraneous intervening DNA since any extraneous intervening HSV sequences in these recombinants are not functioning as a "promoter" and therefore are not a "promoter"). Accordingly, the filing of a Terminal Disclaimer can be considered as to claim 48 after the issues of priority

vis-a-vis Moss et al., and of Moss' patentability vis-a-vis Paoletti are resolved via the Interference.

Additionally, the rejection of claim 40 under Section 103 is overcome by the amendment thereto directing that claim to pDP202 TK/E.

Furthermore, there is no question that the present claims interfere with Moss' claims. More particularly, there is no question that claim 42 interferes with Moss' claim 44, the Count in the Interference.

The Moss arguments for asserting patentability on the basis of "adjacent to", it is submitted, are based upon the deliberate use or placement of a vaccinia transcriptional regulatory sequence (or a vaccinia promoter) to control expression of the foreign gene in a recombinant vaccinia virus along with the foreign gene. Paoletti claims 33 to 51, and particularly Paoletti claim 42, as above-discussed, follow this concept and are therefore the same as, and not broader than, Moss' claims, Moss' arguments, and the present Count.

Paoletti's claims 33 to 51, and claim 42 in particular, define the recombinant vaccinia virus and plasmid therefor in terms of "donor DNA not naturally occurring in vaccinia virus encoding a polypeptide foreign to vaccinia virus" (compare Moss' claim 44 and present Count "first DNA sequence"), and a promoter (compare Moss claim 44 and Present Count subpart (B)). The promoter in Paoletti claim 42 is "operably linked to the donor

DNA ... exerts functional control over the donor DNA ... and, wherein there is expression of the donor DNA under vaccinia control" (Compare Moss claim 44 and Present Count "vaccinia promoter ... wherein ... promoter sequence is adjacent to and exerts transcriptional control over said first DNA sequence"). In claim 42, the "donor DNA [is] present within a non-essential region of a segment of vaccinia virus DNA otherwise co-linear with portions of the vaccinia virus genome such that the donor DNA is positioned within a non-essential region of the recombinant vaccinia virus" (Compare Moss claim 44 and present Count "said segment is positioned within a non-essential region of said recombinant vaccinia virus").

A comparison of terms of Paoletti claim 42 and Moss claim 44 (the Present Count), to show that Paoletti claims 33 to 51 are claiming the same invention as Moss is also set forth in the following Table.

**CLAIM TERM COMPARISON TABLE**

| PROPOSED COUNT A (PAOLETTI CLAIM 42) | PRESENT COUNT (MOSS CLAIM 44) |
|---|---|
| A recombinant vaccinia virus comprising | A recombinant vaccinia virus that comprises a segment comprised of |
| donor DNA not naturally occurring in vaccinia virus encoding a polypeptide foreign to vaccinia virus and | (A) a first DNA sequence encoding a polypeptide that is foreign to vaccinia virus and |
| a promotor operably linked to the donor DNA, and which experts functional control over the donor DNA . . . wherein there is expression of the donor DNA under vaccinia control | a vaccinia promoter sequence wherein (i) said promoter sequence is adjacent to and exerts transcriptional control over said first DNA sequence and |
| said donor DNA present within a non-essential region of a segment of vaccinia virus DNA otherwise co-linear with portions of the vaccinia virus genomic such that the donor DNA is positioned within a non-essential region of the recombinant vaccinia virus | (ii) said segment is positioned within a nonessential genomic region of said recombinant vaccinia virus |

Note again that Moss' "adjacent" is undefined, allows for the presence of extraneous intervening DNA, and, merely mean purposeful placement of a foreign gene and promotor DNA (met by Paoletti's "operably linked . . . which exerts functional control . . . wherein there is expression of the donor DNA under vaccinia control") (See also Moss' functional definition of "promoter" in USSN 07/072,455, page 1, line 22 to page 2, line 5 such that DNA which does not so function, such as any extraneous intervening

HSV TK DNA in vP2, vP4 and vP6 is not a "promoter"; ergo, "adjacent" is satisfied and, Paoletti's "under vaccinia control" language meets Moss' promoter definition). Additionally, if Paoletti '112 Patent claim 7 was designated as corresponding to the Count due to vP22 being recited (despite vP3 and vP5 also recited), then, it is evident that claims 33 to 51 define the same invention as the Count, as shown by Paoletti dependent claims 38, 40, 47, 49 and 50 (AvaI H-fragment, pDP202 TK/E, AvaI H-fragment, vP22, vP9). That is, that claims 38 and 40 can depend from claim 33 and, that claims 47, 49 and 50 can depend from claim 42, further illustrates that Paoletti claims 33 to 51, Proposed Count A (Paoletti claim 42), Moss claim 44 (the present Count) and Moss claims corresponding thereto are all defining the same invention.

The Proposed Count and Paoletti claims 33 to 51 define the same concept or an obvious variant of Moss claim 44, the Count, and Moss' claims corresponding thereto, without the objectionable "adjacent to" phrase. Accordingly, claims 33 to 51 define the same invention as the Count and Proposed Count A (Paoletti claim 42).

Furthermore, as discussed herein, USSNs 06/334,456 and 06/446,824 describe and enable present claims (such as claims 42 and 48) in accordance with 35 U.S.C. §112 so that the claims are entitled to the benefit of these applications.

To be entitled to the benefit of USSN 06/334,456, Paoletti need only show that the application complies with 35 U.S.C. §112, first paragraph with respect to at least one embodiment within the scope of claim 42. See Weil v. Fritz, 196 U.S.P.Q. 600, 608 n.16 (C.C.P.A. 1978). As mentioned above, in the August 31, 1995 Interview, the Examiner agreed that vP2, vP4, and vP6 are three distinct species within claim 42. vP2, vP4 and vP6 are clearly described and enabled in accordance with 35 U.S.C. §112 in USSN 06/334,456 (see, e.g., the Examples in USSN 06/334,456).

Thus, claim 42 and claims corresponding thereto such as claim 48 are entitled to the benefit of USSN 06/334,456; and these claims interfere with Moss' claims.

The application therefore can be passed to the APJ and to the Board so that the application is added to the Interference and the Interference is redeclared with Paoletti as Senior Party (since Moss and Paoletti have interfering claims, and Paoletti is entitled to the benefit of USSN 06/334,456, filed December 24, 1981 - nearly one year before Moss' earliest applications).

And, reconsideration and withdrawal of the Section 102 and 103 rejections, and the passing of the application to the APJ and the Board for its addition to Interference No. 103,399 with the Interference redeclared with Paoletti as Senior Party, are respectfully requested.

**2. There Is No Requirement In The Law For "Blazemarks"; And The Claims Are Described And Enabled Under Section 112 In USSNs 06/334,456 And 06/446,824, As Set Forth In The March 16 Amendment**

Copies of motions made in the Interference were provided to inform the Examiner of issues pending before the APJ and the Board by the Interference. Copies of Declarations were provided to introduce facts into the record. A copy of additional Declarations in the Interference by Drs. Dennis Hruby and Enzo Paoletti are attached as Exhibits A and B. Full consideration of the Declarations of Drs. Hruby and Paoletti is earnestly solicited.

The Office Action fails to accord the benefit of USSN 06/334,456 and 06/446,824 to the claims, asserting that "there is no written description ... since there are no blazemarks to vaccinia promoters that exert functional control over the donor DNA."

As to USSN 446,824, in addition to vP22, and Examples XXIV and XXV, attention is directed to Figs. 9A to 9C, Examples XIV to XVIII, vP9, and col. 16, line 47 to col. 21, line 29 of the '112 Patent. More particularly, vP9 contains the influenza HA gene. The preparation and expression of vP9 is detailed in Examples XIV to XVIII and col. 16, line 47 to col. 21, line 29. That an endogenous vaccinia promoter exists in the F-fragment

used in vP9 (as well as in vP2, vP4 and vP6), as well as its tentative site therein is disclosed in Figs. 9A to 9C.

Accordingly, USSN 446,824 demonstrates expression of exogenous DNA without the non-vaccinia promoter thereof being present with respect to HSV TK in the AvaI H-fragment and with respect to influenza HA in the F-fragment; and, the latter, especially in conjunction with vP1, vP3 and vP5, as well the former, clearly demonstrate that expression in vP2, vP4 and vP6 is from the endogenous vaccinia promoter in the F-fragment.

Thus, there is indeed written description of "expression under vaccinia control", and guidance as to how to obtain additional control regions.

Moreover, that expression in vP2, vP4, vP6, vP9 and vP22 is under vaccinia control is inherent; and, that which is inherent need not be explicitly stated in the application.

In this regard, attention is respectfully directed to Kennecott Corp. v. Kyocera International, Inc., 5 U.S.P.Q.2d 1194 (Fed. Cir. 1987) and In re Wertheim, 191 U.S.P.Q. 90 (C.C.P.A. 1976). In Kennecott the '299 patent issued from a continuation-in-part application that contained a substantial portion of the '954 parent application, plus a description of and photomicrographs showing the equimaxed microstructure. The '299 patent claims contain the words "equimaxed microstructure" that were not present in the '954 parent application. The claims were

accorded the benefit of the parent application and, the Federal circuit held:

> By disclosing in a patent application a device that inherently performs a function, operates according to a theory, or has an advantage, a patent applicant necessarily discloses that function, theory or advantage even though he says nothing concerning it.

5 U.S.P.Q.2d at 1197 (citing In re Reynolds, 170 U.S.P.Q. 94, 98 (C.C.P.A. 1971), quoting Technicon Instruments Corp. v Coleman Instruments, 150 U.S.P.Q. 227, 236, (N.D. Ill. 1966), aff'd, 155 U.S.P.Q. 369 (7th Cir. 1967)). See also Kennecott, 5 U.S.P.Q.2d at 1198 (inclusion of inherent property in later-filed claims does not deprive benefit of earlier filing date).

It cannot be denied that vP2, vP4 and vP6 inherently meet the recitation of claim 42. Nor can it be denied that the plasmids from which vP2, vP4 and vP6 originated inherently meet the recitation of claim 33. Under Kennecott, claims 33 and 42 are entitled to the benefit of USSN 334,456. See also Wertheim at 191 U.S.P.Q. 96:

> The function of the description requirement is to ensure that the inventor had possession, as of the filing date ...; how the specification accomplishes this is not material. In re Smith ... 178 U.S.P.Q. 620 (CCPA 1973) ... It is not necessary that the application describe the claim limitations exactly ... but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations.

It is clear from comparing vP2, vP4 and vP6 versus vP1, vP3 and vP5, and the plasmids from which these recombinants originated, and the entire disclosure of the '330 Patent (including teaching of use of "strong promoter" and "expression under vaccinia control") that the skilled artisan would recognize that Paoletti et al, in USSN 334,456 invented the products of claims 33 and 42.

As to USSN 334,456, the application clearly teaches "expression under vaccinia control" ('330 Patent, col. 10, line 10). The statement at column 10, lines 6 to 10 of the '330 Patent is unequivocal! Both replication and expression by the "vaccinia variants" is "under vaccinia control". The Office Action at page 5 attempts to improperly dissect the statement.

Furthermore, the overall teachings of USSN 334,456 demonstrate that the claims are supported therein. As a first point, at column 8, line 64 through column 9, line 5, the premise of vP1, vP3 and vP5 versus vP2, vP4 and vP6 is set forth; namely, that these two sets of recombinants were created so that expression would indicate whether the HSV promoter sites were operational, or whether a promoter site within the F-fragment itself was operational. That there is one of two possibilities is not equivocal.

For instance, the undersigned photocopied each side of a typical U.S. quarter dollar coin ("quarter"), at 400 x enlargement, and each of those photocopies is attached as

Exhibits C and D. To paraphrase USSN 334,456, both photocopies are attached, each respectively as Exhibits C and D, so that an image of "heads" may occur no matter in which Exhibit it occurs. In other words, there is certainly a "heads" in either Exhibit C or Exhibit D, and, the undersigned has described both "heads" and "tails" by attaching Exhibits C and D. To ascertain whether Exhibit C is "heads", one need only turn to Exhibit C - if it is "heads", then Exhibit D, as a matter of fact must be "tails". And likewise, if Exhibit D is "tails", Exhibit C as a matter of fact must be "heads". There is no equivocation when an event must occur only as a result of one of two possibilities, and both possibilities and the result are disclosed.

By providing "heads" as one of two disclosed possibilities, the undersigned, like Applicants in USSN 334,456, had fully described both possibilities. Likewise Applicants have provided a sufficient description of expression under vaccinia control for written description and enablement purposes by describing vP1, vP3, vP5 and vP2, vP4 and vP6. More specifically, the results of no expression by vP1, vP3 and vP5, in contrast to expression by vP2, vP4 and vP6, together with the statements at column 8, line 64 through column 9, line 5, column 10, lines 6 to 10, and column 28, lines 10 to 18 of the '330 Patent demonstrate that: Applicants recognized that expression would be from one of two possibilities (either from the HSV promoter sites or endogenous promoter with F-fragment), both

possibilities were disclosed as well as the result (vP1, vP3, vP5, and vP2, vP4, vP6, and expression by vP2, vP4, vP6); and "expression under vaccinia control" was the conclusion by Applicants (and, it was also inherent in vP2, vP4 and vP6). Note also the disclosure of using a strong promoter in USSN 334,456 (such that Applicants recognized that expression under vaccinia control was from a promoter).

Furthermore, during the August 31, 1995 Interview, the Examiner agreed that vP2, vP4, and vP6 are three distinct species within claim 42. Certainly three species is sufficient to enable the generic concept of claim 42. However, during the August 31, 1995 interview the Examiner inquired as to how the skilled artisan at the time of USSNs 06/334,456 and 06/446,824 would ascertain other non-essential regions and other promoters.

With regard to USSN 06/446,824, by way of reference to the '112 Patent, it is asserted that the '112 Patent teachings includes the introduction of pBR 322 into vaccinia virus to generate vP7 and vP8 and the construction therefrom of vP10, vP13, vP14 and vP16, the TK deficient vaccinia virus VTK-79, and the use of the Ava I H fragment for generating vP22; and, it is further asserted that these teaching describe and enable non-essential regions other than the HindIII F-fragment in accordance with 35 U.S.C. §112 (note particularly that the teachings of constructing vP7, vP8, vP10, vP13, vP14, and vP16 describe and enable synthetically made non-essential regions by means of

recombination, the teachings of the TK deficient vaccinia virus describe and enable the TK region as a non-essential region, the teachings of the construction of vP22 describes and enables the Ava I H region as non-essential, such that USSN 06/446,824 contains a disclosure in accordance with 35 U.S.C. §112 of at least four (4) different types of non-essential regions; see also discussion below of teachings of the '330 Patent which are contained within the '112 Patent such that at least a fifth non-essential region is also described and enabled in accordance with 35 U.S.C. §112).

Further, it is noted that the '112 Patent claims employ the term "non-essential region" such that the PTO has already deemed the term sufficiently described and enabled in accordance with 35 U.S.C. §112 by the PTO (such that it is respectfully submitted that for the Examiner to now attempt to assert any Section 112 issue with respect to the term requires approval thereof by at least the Group Director).

With regard to USSN 06/334,456, it is noted, by way of the '330 Patent that the claim term "non-essential region" has already been deemed sufficiently described and enabled in accordance with 35 U.S.C. §112 by the PTO, as shown by claims 3 and 8 of the '330 Patent using the term (such that it is respectfully submitted that for the Examiner to now attempt to assert any Section 112 issue with respect to the term requires approval thereof by at least the Group Director).

Moreover, not only does the '330 Patent disclose the Hind III F-fragment region as non-essential, but also the '330 Patent discloses the TK deficient vaccinia virus VTK-79, such that the TK region is also disclosed as non-essential. Additionally, the '330 Patent teaches at column 3, lines 8 to 28):

> Since the central portions of the DNA of all pox viruses are similar, while the terminal portions of the viruses differ more strongly, the responsibility of the central portion for functions common to all viruses, such as replication, is suggested, whereas the terminal portions appear responsible for other characteristics such as pathogenicity, host range, etc. If such a genome is to be modified by the rearrangement or removal of DNA fragments therefrom or the introduction of exogenous DNA fragments thereinto, while producing a stable viable mutant, it is evident that the portion of the naturally-occurring DNA which is rearranged, removed, or disrupted by the introduction of exogenous DNA thereinto must be non-essential to the viability and stability of the host, in this case the vaccinia virus. **Such non-essential portions of the genome have been found to be present in the WR strain of vaccinia virus, for instance within the region present within the L-variant but deleted from the S-variant or within the Hind III F-fragment of the genome** [emphasis added].

Thus, clearly at least three different non-essential regions are described and enabled in accordance with 35 U.S.C. §112 in USSN 06/334,456. Furthermore, the '330 Patent, at column 14, lines 51 to 62 teaches and enables, in accordance with 35 U.S.C. §112, the use of inserting exogenous DNA "into various portions of the vaccinia genome for purposes of identifying non-

essential portions of the genome." That is, according to the '330 Patent, if the exogenous DNA can be inserted into the vaccinia genome as it is in the Hind III F-fragment thereof, "the region of the genome into which it has been introduced is evidently non-essential." In this manner: "[e]ach non-essential site within the genome is a likely candidate for the insertion of exogenous genes so that the methods of the present invention are useful in mapping such non-essential sites in the vaccinia genome."

Thus, not only has the claim term "non-essential region" already been accepted by the PTO, but moreover, USSNs 06/334,456 and 06/446,824 teach and enable a plurality of non-essential regions, as well as means for identifying other non-essential sites in the vaccinia genome.

With respect to promoters, reference is made to the Paoletti and Hruby Declarations and the documents they cite. For instance, Weir et al., PNAS USA 79: 1210-1214 (February 1982), Hruby 1982, J. Virology 43(2):403-409 (August 1982), Venkatesan et al., Cell 125:805-813 (September 1981), Molecular Biology of the Gene, p. 714 (3d Ed. by James Watson, 1976) (a standard textbook), Pribnow, "Genetic Control Signals in DNA", ch. 7 in Volume 1, "Gene Expression" of Biological Regulation and Development (edited by Robert F. Goldbeyer) ("Pribnow"), 1980, especially Sections 2.1, "The Transcript Unit", and 3.1, "The Promoter," p. 230, 231, Rosenberg and Court (1979), "Regulatory

sequences involved in the promotion and termination of RNA transcription," Ann. Rev. Genetics 13:319-353, Breathnach and Chambon (1981), "Organization and expression of eucaryotic split genes coding for proteins," Ann. Rev. Biochem. 50:349-383, Moss et al., "Deletion of a 9,000-Base-Pair Segment of the Vaccinia Virus Genome that Encodes Nonessential Polypeptides," J. Virol., 1981, 40: 387-95, Panicali et al., "Two Major DNA Variants ...", J. Virol., 1981, 37:1000-1010 ("Panicali et al. 1981") and Hruby et al., J. Virol. 1981, 40: 456-64 ("Hruby 1981"), relevant art, which can be read with USSNs 06/334,456 or USSN 06/446,824. Mention is also made of Hruby et al., 1981, "Cell-free synthesis of enzymatically active vaccinia virus thymidine kinase," Virology 113:594-601, a copy of which, or of any of the other cited documents, will be provided upon request (as it is assumed that the Examiner has access to all of the aforementioned documents)

Note the disclosure of Panicali et al. 1981 in view of the disclosure of Moss et al. 1981, wherein Moss et al. confirm the observations of Panicali et al. 1981 and, which at 394 states:

> The deletion described here appears to be very similar to the one recently reported by Panicali et al. (17) in a stable "small DNA" variant. Indeed, we suspect that it is identical since their serially passaged stock was obtained originally from our laboratory.
>
> The deletion within the vaccinia virus genome had no apparent effect on specific

> infectivity or virus yield in HeLa cells or plaque size in BSC-1 cells (14). Our preliminary experiments also indicated that variant 6/1 and 6/2 replicated in pig kidney cells (kindly supplied by R. Moyer) in contrast to the host range effects seen with some rabbitpox deletion mutants (16). Therefore, it was of particular interest to determine whether the deletion was in a silent or expressed region of the vaccinia virus genome. Blot hybridization studies of Panicali et al. (17) suggested that the region is an immediate early or early transcriptional unit. Recent translational and transcriptional maps of the left side of the genome reproduced in Fig. 5 indicated that the deleted region encodes a minimum of seven or eight immediate early as well as two minor late polypeptides (4, 25). In this report, the absence of all of these early mRNA's in cells infected with the deletion mutant was established by cell-free translation experiments.

As shown by Moss et al. 1981 and Paoletti et al. 1981, the vaccinia genome was known to contain numerous promoters. Note, for instance, that in one region of the vaccinia genome Moss et al. 1981 confirmed that it was "an immediate early or early transcriptional unit [which] ... encodes a minimum of seven or eight immediate early ... polypeptides."

As shown in Pribnow, Section 2.1 at p.230 a "transcriptional unit is a stretch of DNA base pairs bounded on one end by a 'start sequence' or *promoter* ... and the other end by a 'stop sequence' or *terminator* "(emphasis in original).

It is important to note that the 5' region containing the RNA start site of the vaccinia gene encoding the 7.5 Kd polypeptide is the vaccinia 7.5 K promoter. Thus, the sequence

of the 7.5 K promoter was disclosed in Venkatessan. No further information other than the information disclosed in Venkatessan was required to obtain the vaccinia 7.5 Kd promoter, as shown in the following discussion.

A standard textbook published in 1976 defines a promoter as a "[r]egion on DNA at which RNA polymerase binds and initiates transcription" (p. 714, Molecular Biology of the Gene, 3rd edition, by James Watson). Similarly, in 1980 David Pribnow stated "The basic promoter is only that particular DNA sequence that is recognized directly and used by the RNA polymerase as a start signal for transcription" (Pribnow 1980, section 3.1 "The Promoter", p. 231).

The nature of and elements contained within both procaryotic and eucaryotic promoters were well defined before the filing dates of USSNs 06/334,456 and 06/446,842 (Rosenberg and Court, 1979; Pribnow 1980; Breathnach and Chambron, 1981). In particular, it was well established that promoters are commonly located upstream from the ATG initiation of translation sites which begin DNA sequences coding for proteins.

In Venkatessan the authors demonstrate extensive familiarity with this knowledge in the state of the art by citing and discussing several publications which reveal elements and characteristics of various procaryotic and eucaryotic promoters (Rosenberg and Court, 1979; Pribnow 1980; Benoist et al., 1980; Flavell et al., 1979; Canaani et al., 1979; Baker et al., 1979;

Hashimoto and Green, 1980). The authors of Venkatessan also discuss the occurrence of sequence motifs near the potential AUG initiation of translation sites in the 7.5K mRNA which are similar to sequence motifs found near the initiation of translation codons found in various other virus RNAs (vesicular stomatitis virus RNA, alfalfa mosaic virus RNA 4: Rose 1978; late adenovirus mRNA: Ziff and Evans, 1978; turnip yellow mosaic virus mRNA: Briand et al., 1978).

In its title (p. 805) Venkatessan disclosed, "distinctive nucleotide sequence adjacent to multiple initiation ... sites of an early vaccinia virus gene" (i.e., the 7.5 Kd gene; emphasis added).

The summary of Venkatessan (p. 805) includes the following:

> A remarkable 88% AT-rich 60 bp DNA sequence was found immediately upstream of the initiation of transcription sites. Although DNA sequences that bear some homology to Pribnow and Hogness boxes are present, additional recognition sequences located further upstream of procaryotic and eucaryotic initiation sites are absent. A possible initiation of translation codon occurs about 50 nucelotides from the 5' end of the message.

The preceding quote clearly describes sequence characteristics of the 7.5 promoter, in comparison to the sequences of canonical procaryotic promoters (which contain a Pribnow box) and eucaryotic promoters (which contain a Hogness box). As the authors in Venkatessan note (p. 810).

> AT-rich sequences previously have been found within the promoter regions of procaryotic and eucaryotic mRNAs

> AT-rich region near the viral initiation of transcription site showed some homology to similar regions of procaryotic and eucaryotic genomes, additional homology was not found further upstream.

In Venkatessan the authors further note (p. 805), col. 1. lines 7-14) that

> Recently several mRNAs made early after vaccinia virus infection ... and in vitro by virus cores (Venkatesan and Moss, 1981) have been mapped on the vaccinia virus genome. These early mRNAs are not spliced and their cap structures retain the $\beta$-$^{32P}$-label of the initiating nucleotide, indicating the absence of processing at the 5'-end.

As the authors of Venkatessan stress (p. 809), referring to the mRNA for the 7.5 polypeptide,

> the $\beta$-phosphate of GTP previously was shown to be incorporated into cap structures of this mRNA, providing evidence of the strongest kind that the 5' ends represent true initiation sites (Venkatesan and Moss, 1981)

(i.e., that the 5' end of the mRNA maps to the 7.5 K promoter region).

Finally, (at p.811) the authors of Venkatessan conclude

> The multisubunit RNA polymerase of vaccinia virus, like that of procaryotic and eucaryotic organisms, must be capable of interacting with the promoter sequences for a large number of RNAs. Efforts to extend the present studies by sequencing additional genes are in progress.

It is thus evident that the DNA sequences disclosed in Venkatessan around the 5' end of the mRNA for the 7.5 polypeptide are in fact and were at the time of publication thereof known to be the promoter sequences for the 7.5 K gene.

Thus, the Venkatessan, and Panicali et al. 1981 or Moss et al. 1981 placed into the skilled artisan's hands several promoters, including the 7.5 promoter, prior to the filing dates of USSNs 06/334,456 and 06/446,842.

Hruby et al 1981 describes the control of expression of the vaccinia virus TK gene, and the Hruby et al. Virology article describes cell-free expression of vaccinia virus TK. Certainly prior to the filing dates of USSN 06/334,456 and 06/446,842, the skilled artisan had the TK promoter in his hands (and, by the disclosure of the TK deficient vaccinia virus in USSNs 06/334,456 and 06/446,842, the skilled artisan thus had a non-essential region and knowledge of its endogenous promoter thereat).

Weir et al. discloses that "the vaccinia thymidine kinase gene maps to the 5,000 bp HindIII J fragment". The person of skill in the art, who wished to obtain a vaccinia TK promoter would naturally focus his search to sequences within the vaccinia HindIII J fragment. The person of skill in the art would expect that the TK promoter would be located in upstream sequences of the TK gene. In Weir et al. the authors acknowledge that they were not the only group that had mapped the TK gene to HindIII J (p. 1210, col. 2, lines 30-34): "Further evidence that the HindIII J fragment contains the structural TK gene was obtained in our laboratory and in that of D.E. Hruby and L.A. Ball (personal communication) by cell-free translation of

hybridization selected mRNA under conditions suitable for expression of active TK."

Drs. Ball and Hruby, in Hruby 1982, reported in detail the location of the vaccinia TK gene. In Hruby 1982, Drs. Ball and Hruby were the first to report that the vaccinia TK gene was transcribed as a 700 nt RNA, and that, contrary to previous expectations, the gene encoded a 19 kilodalton protein. They also reported that "the tk gene lies completely within HindIII fragment J, and this conclusion is supported by recent analyses of subfragments of J, which show that the gene lies between about 0.5 and 1.2 kilobases from the L-J boundary". They also disclosed that "the structural gene for VVtk is located in HindIII fragment J at 42.5 to 45.1 map units".

Thus, prior to the filing dates of USSNs 06/334,456 and 06/446,842, information was available in the public domain which could be used by persons of skill in the art to obtain the vaccinia TK promoter, without any inventive efforts. Note also Hruby et al. 1981, and the Hruby et al. Virology article.

Thus, from the disclosure of either USSNs 06/334,456 or 06/446,842, and the knowledge in the art, the skilled artisan could easily, without inventive effort, select non-essential regions other than the Hind III F-fragment region and promoters other than the F7L promoter, such that claim 42 is fully described and enabled in each of USSN 06/334,456 and 06/446,842,

in accordance with 35 U.S.C. §112, such that claim 42 should clearly be accorded the benefit of each of these applications.

Additionally, Applicants' direct the Examiner's attention to the Preliminary Amendment by Moss et al. in USSN 07/987,546 which states in pertinent part (at pages 9 to 15, emphasis added):

> The examiner has additionally argued that **under §112, first paragraph, the claims should be limited to the promoters which are exemplified** ...
>
> Applicants vigorously traverse this rejection for the following reasons: ...
>
> (2) ... **the examiner's own art demonstrates that precise RNA mapping and sequencing was well within the skill of the art at the time of the invention**; ...
>
> [T]he examiner questions whether "the ordinary skill in the art extends to precise mapping of any RNA start codon and sequencing" ... . In response, applicants direct the examiner to her own art, Wittek et al., Cell 21:487-493 (1980), which provides a detailed analysis of individual poxvirus mRNAs conducted and published well before the present application's effective filing date.
>
> Other references ... provide similar guidance with regard to precise mapping of RNA start codons. For instance, Weaver and Weissman, Nucleic Acids Research 7(5):1175-1193 (1979), describe a general method of mapping any RNA start site by labeling the 5' end of a DNA segment with 32p hybridizing the labeled DNA to nRNA, digesting the unhybridized regions with a single-stranded nuclease such as S1 and analyzing the protected probe by polyacrylamide gel electrophoresis alongside a sequence ladder. The method was refined by Green and Roeder, Cell 22:231-242 (1980). A general method of

sequencing any DNA was reported by Maxam and Gilbert, Proc. Nat'l Acad. Sci. USA 74(2):560564 (1977). **These methods were used by Venkatesan, Cell 125:805-813 (1981), and J. Virol. 44(2):637 (1982), prior to the filing date of the present application.** Essentially similar procedures were subsequently used to determine the 5' ends of dozens of vaccinia virus nRNAs. See, e.g., Lee-Chen et al., Virology 163:64-69 (1988); Rosel and Moss, J. Virol. 56:830-838 (1985); Rosel et al., J. Virol. 60:436-39 (1986) and Weir and Moss, J. Virol. 51:662-669 (1984). **In view of this art, the examiner has arguably not focused on what was available at the time of the invention in concluding that "much remained to be learned about promoters in 1982".**

It is assumed that the Examiner can access the documents Moss et al. cited in overcoming the same issue presented during the August 31, 1995 Interview. Moreover, the above-quoted portions of arguments by Moss et al. are applicable in the present case. At the time of USSNs 06/334,456 and 06/446,842, much was known about vaccinia virus promoters such that no undue experimentation was required at the filing dates of those applications to practice claim 42.

Also, mention is made of the teachings of constructing vP22 in the '112 Patent. Since the exogenous DNA was inserted into the Ava I H-fragment and is clearly taught as being under the control of the endogenous vaccinia promoter, clearly USSN 06/446,842 taught and enabled at least two promoters.

Therefore, no further "blazemarks" are required under Section 112. And, this leads to Applicants' second point; namely, that there is no basis in law for requiring "blazemarks".

The first paragraph of Section 112 relates not to the form or content of the claims in an application but to the content of the specification. It states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In this case, as pointed out above, there is an exact correspondence between the claim language and the original specification disclosure so that the description requirement is clearly satisfied.

There is, of course, no reference to "blazemarks" in any paragraph of 35 U.S.C. §112 and, based upon a search for cases in which that term appears, two decisions by the Court of Customs and Patent Appeals were found. Neither of those cases is pertinent here.

The first reported decision in the Court of Customs and Patent Appeals in which the term "blazemarks" appears is In re Ruschig, 154 U.S.P.Q. 118 (C.C.P.A. 1967). In that case, the

appellant, Ruschig, has added to his application a species claim from another application directed to a single compound, i.e., N-(p-chlorobenzenesulfonyl)-N'-propylurea. Ruschig's specification contained generic descriptions of various classes of compounds which would include the claimed compound but there was no description of that particular compound in the specification. Because the claim on appeal was directed to a single compound, the Court upheld the PTO rejection stating, at 122:

> Specification claims to single compounds require reasonably specific supporting disclosure and while we agree with the appellants, as the board did, that naming is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required. Surely, given time, a chemist could name (especially with the aid of a computer) all of the half million compounds within the scope of the broadest claim, which claim is supported by the broad disclosure. This does not constitute support for each compound individually when separately claimed. (Emphasis added.)

The Court rejected Ruschig's argument that a broad description of a process for making the class of compounds, which included a generic description of ingredients, provided support for the claim since that description suggested the ingredients necessary to make the claimed compound stating, at 122:

> Next, it is argued in connection with these processes that in the discussion of Process (1) it is taught that the primary amine could be "a primary butylamine or another primary alkylamine or an

> alkenylamine, cyclo-alkylamine or cycloalkylalkylamine containing 2 to 7 or 8 carbon atoms" and that one skilled in the art could see that "if n-butyl-amine is a reactant, then ethylamine, n-propylamine, etc., are also possible reactants." We do not see that this guides one to the use of n-propylamine. The important words in the quotation from our point of view are "etc." and "possible".

The Court then went on to express the rationale for its determination. It pointed out that generic or class descriptions of large groups of compounds are insufficient to provide supporting disclosure for a single compound within that class or group which is not specifically described, stating, at 122:

> It is an old custom in the woods to mark trails by making blazemarks on the trees. It is no help in finding a trail or in finding one's way through the woods where the trails have disappeared -- or have not yet been made which is more like the case here -- to be confronted simply by a large number of unmarked trees. Appellants are pointing to trees. We are looking for blazemarks which single out particular trees. We see none.

Another reported decision by the Court of Customs and Patent Appeals in which the term "blazemarks" appears is In re Arkley, 172 U.S.P.Q. 524 (C.C.P.A. 1972). In that case, as in Ruschig, the appealed claim was drawn to a single compound, i.e., a particular cephalosporin A-type compound called cephalosporin. The prior art patent to Flynn, upon which the rejection of the claim had been based, was directed to cephalosporin C compounds and merely disclosed a general procedure by which cephalosporin C could be converted into cephalosporin A compounds. The Flynn

patent included a broad disclosure of a class of cephalosporin C compounds having a basic structural formula with four variant groups which encompassed over 230,000 cephalosporin C-type compounds.

In reversing the PTO rejection of the appealed claim based on the disclosure of the Flynn patent, the majority in Arkley concluded that the Flynn patent did not disclose the "blazemarks" of the type referred to in Ruschig which would assist one skilled in the art in selecting a specific compound of one type from the generic disclosure of a class of compounds of a different type.

Chief Judge Worley, however, dissented from the holding of the majority, pointed out that the disclosure in the Flynn patent of cephalosporin C compounds would normally lead one skilled in the art to prepare cephalosporin A analogs including the compound of the appealed claim, stating, at page 530:

> I think it is clear that Flynn directs one of ordinary skill in the art, who is interested in particular cephalosporin $C_A$ analogues of the 37 or so cephalosporin C type compounds Flynn specifically discloses, to prepare them by reacting the appropriate 7-acylamido cephalosporanic acid with the particular tertiaryamine pyridine. Following those instructions, one of ordinary skill in this art would easily prepare the $C_A$ (pyridine) analogue of the particular cephalosporin C type compound described in Examples 4 and 10, which analogue is cephaloridine. Each and every one of the $C_A$ (pyridine) analogues of that relatively small number of cephalosporin C compounds has been effectively, or implicitly, described by

> Flynn. To be sure, appellant is claiming only one of them, but it is no less described that any of the others. (Emphasis added).

Chief Judge Worley commented on the failure of the majority opinion to recognize the "blazemarks" which were present in the Flynn patent as had been understood by the PTO in its rejection of the appealed claim. He concluded that the particular things, or "blazemarks", from which one of ordinary skill in the art would perceive the invention of the claim on appeal were clearly present in the Flynn patent, stating at page 530:

> The principal opinion also criticizes the board for reading into references "things that are not there." My difficulty with that position stems from its disregard for the "things" --or "blazemarks" --that are there. (Original emphasis).

Thus, the cases in which the Court of Customs and Patent Appeals has applied the term "blazemarks" in connection with an interpretation of 35 U.S.C. §112 were cases in which the appealed claim was directed to a single compound not specifically disclosed or suggested in the specification or prior art reference of interest where the question was whether one skilled in the art would be led to the specific compound of the appealed claim as a result of the disclosure of a class of similar compounds. In such cases, the Court found that the selection of a single, undisclosed compound was akin to the identification of a single tree in a large forest and required "blazemarks" to

assist those skilled in the art to find their way through the forest to the location of the single tree of interest.

That rationale is obviously inappropriate in this case. Here the subject of interest is a large subsubgeneric class of recombinant vaccinia viruses comprising donor DNA not naturally occurring in vaccinia virus encoding a polypeptide foreign to vaccinia virus and a promoter operably linked to, and exerting functional control over, the donor DNA (the generic concept of a recombinant vaccinia virus and the subgeneric concept of a recombinant vaccinia virus wherein the DNA is expressed, claims 1 and 2 of the '112 Patent, not being in issue as Moss has never attempted to claim these concepts). This subsubgeneric class corresponds to an entire forest, and not merely one species corresponding to a single tree. No "blazemarks" are necessary to identify the forest, which can clearly be selected and observed without difficulty (since its selection is the same as selecting "heads" from Exhibits C and D).

Consequently, there is no requirement for "blazemarks" in the law; the "blazemarks" called for by cases using that term are not applicable in the present case; but, even if they were, all of the appropriate "blazemarks" are included in USSN 334,456 and 446,824, which unquestionably described and enable the skilled artisan to practice the claimed invention.

Accordingly, the rejection should be withdrawn; the claims should be accorded the benefit of USSN 334,456 and

446,824; the application should be added to the Interference (with Paoletti as Senior Party); and, such relief is respectfully requested.

Nonetheless, in view of M.P.E.P. 2309.02, and the motions pending, the issue of entitlement to the benefit of USSN 334,456 and 446,824 is before the APJ and the Board. Therefore, the Office Action and its finality should be withdrawn, and such relief is respectfully requested.

**CONCLUSION**

In view of the foregoing, consideration and entry of this Amendment, withdrawal of the Office Action and of its finality, addition of this application to the Interference with claims 33 to 51 designated as corresponding to the Count, substitution of the Count with Claim 42, and redeclaration the Interference with Paoletti as Senior Party, are respectfully requested.

Respectfully submitted,

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